

**Submission
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**INQUIRY INTO USE OF PRIMATES AND OTHER ANIMALS
IN MEDICAL RESEARCH IN NEW SOUTH WALES**

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Submission to New South Wales Parliament Inquiry into the use of primates and other animals in medical research in New South Wales.

Dear Committee members

I am a 67 year old retired Australian born GP with a background in maternal – child health and public health. I was formerly an HIV / AIDS Co-ordinator for the Western NSW Public Health Unit (1994); and the last GP obstetrician in Cobar (1995-2006). I've spent over half my medical career in rural and remote locations in PNG, outback Australia and rural South African locations.

Over the past 40 years, I have witnessed the triumphs and failures of biomedical research at the coalface~ Neonatal and child ICU to remote outback clinics. To admit a patient to Cobar Hospital, suffering a myocardial infarction ~ dissolving a potential lethal clot in his coronary artery, and shipping my fellow citizen to the Royal North Shore Hospital for stenting and return to Cobar Hospital on the mend within 24 hours is a fantastic achievement. To deny such technological and human achievements would be churlish.

And yet, the commercialisation and corporatisation of biomedical research backing these achievements has an unsavoury underbelly. A lack of transparency, accountability, informed consent and indeed justice prevail in our biomedical research culture. This week, the prestigious journal Nature reports “A quarter of medical researchers involved in clinical (Human) trials in Australia did not declare funding from pharmaceutical companies.”¹ Declaring conflicts of interest in Australia relies on an honour system. “This is not an issue of weeding out a few bad apples,” co-lead author Associate Professor Barbara Mintzes from Sydney University says. “Based on our findings, the issue of incomplete and inaccurate disclosure is widespread.”²

This report simply re-confirms the widespread acknowledgment that extensive industry influence is undermining “the integrity of scientific investigations, the objectivity of medical education, the quality of patient care, and the public’s trust in medicine.”³

¹ Clare Watson. Undisclosed industry payments rampant in drug trial papers. Nature news 24th March 2022.

² Lucy Carroll and Liam Mannix. The Sydney Morning Herald March 13, 2022.

³ Ray Moynihan et al. BMJ 2019;367: 16576 doi: 10.1136/bmj.16576

What has this to do with Animal Research?

Animal research has been considered the cornerstone of biomedical research; proponents claiming the benefits to humans are self-evident. This is not supported by evidence.⁴ The Collaborative Approach to Meta-Analysis and Review of Animal Data from Experimental Studies (COMRADES) compelled John Ioannidis ~ Professor of Health Research and Policy at Stanford University to comment on the serious bias in animal studies such that “it is nearly impossible to rely on most animal data to predict whether or not an intervention will have a favourable clinical benefit-risk ratio in human subjects.”⁵

Many promising findings from animal research fail in human trials. It is argued that the narrow reductionist approach of biomedical research fails because it relies on animal models in the lab, which fail to reproduce the biological, psychological and social relationships which impact the ecology in which human disease and indeed health evolve.

The “Focus on the model and not the disease” approach in Alzheimer’s research epitomised the limitations and indeed failure of this approach. ⁶ Billions of dollars have been wasted and millions of animals needlessly sacrificed chasing the dominant scientific hypothesis “the Beta-Amyloid hypothesis” for Alzheimer’s dementia, which after forty years has been found wanting. We still have no cures, and little reflection on the cause of this waste of life and precious research dollars.

Humans and animals be they lab rats, baboons or pigs share a common evolution, but differing trajectories have ultimately led to differing physiology, leading to differences in drug metabolism, explaining in part the failure of most pre-clinical (Animal) trials in leading to effective clinical outcomes in humans.⁷ The failure rate of pre-clinical animal research translating into effective clinical therapies has been conservatively estimated as 96%.⁸ Is this really good enough? Is this a good use of scarce research dollars?

Over the past decade, the CRISP-R gene editing technology has been deployed to edit genomic DNA (our genetic heritage) with lab RNA (the messenger).

⁴ Pandora Pound and Michael Bracken. Is animal research sufficiently evidence based to be a cornerstone of biomedical research ? BMJ 2014 ; 348
doi:<https://doi.org/10.1136/bmj.g3387>

⁵ Ioannidis JPA Extrapolating from animals to humans. Sci.Trans Med 2012; 4, 1-

⁶ Susan Fitzpatrick. Asking the right questions in Alzheimer’s research. Issues in Science and Technology. Fall 2018

⁷ Greek R, Menache A. Systemic reviewer of animal models: methology versus Epistemology. Int J Med. Sci. 2013; 10:206-21

⁸ Pippin J. Animal research in medical sciences: Seeking a convergence of science, medicine and animal law. South Texas Law Review 2013; 54:469-511

Invariably describe as a “Genetic scissors”, this technology had been in clinical application for a very short period of time, and the jury is still out as to medium to long-term safety. Is this good enough? Are we proceeding with due diligence?

CRISP-R (Clustered Regularly Interspaced Short Palindromic Repeats) is considered a game changer and allowed Xenotransplantation research to proceed at pace. But is the benign portrayal of CRISP-R gene editing as a precision intervention accurate? Some researchers caution that “focal” edition of DNA may affect the whole genome as it behaves as an “All” in harmony with each of our 24 chromosomes. Removal of a knot in a knitted garment may lead to an unravelling of the whole; thus the legitimate concerns of many scientists about so called “off-target” effects ~ the potential for collateral damage of our genome.⁹

Clinical XENOTRANSPLANTATION, the transplantation of cells, tissues or organs from non-humans to humans, crosses a species barrier that has evolved over millions of years. We violate this evolutionary boundary at our collective peril.

Xenotransplantation research at the Sydney University (Royal Prince Alfred Hospital and Westmead Hospital) is the most egregious example of all that is wrong with biomedical research in NSW/ Australia. RPAH and Westmead Hospital have been carrying out controversial xenotransplantation research for over two decades. This unethical research on primates – baboons and pigs involves the laboratory creation of hybrid primate-pig organs to be grown in surrogate genetically modified pigs. Precise technical details are “Commercial in confidence.” The baboons have reached their use by date and we are on the cusp of clinical trials.

Lack of transparency, lack of informed societal consent and conflict of interest have bedevilled this research for two decades. There has been little if any real public consultation, according to three experts reporting on this: Professor Peter Collignon- ANU; Professor Peter Sainsbury – Sydney University/ Australian Health Ethics Committee (ret.) and Professor Anne Keogh a cardiologist at St Vincent’s Hospital.¹⁰

In 2018, the NHMRC updated the 2007 National Statement on the Ethical Conduct of Human Research, providing a permissive framework for clinical xenotransplantation trials to proceed.¹¹ Major ethical concerns have been voiced and ignored in Australia. Professor Peter Collignon, an ANU based Public Health expert, and NHMRC consultant opined in 1998:

⁹ Heidi Ledford. CRISP-R Babies ~ When will the world be ready? Nature 20 June 2019.

¹⁰ Anna Salleh. Dissent over animal to human transplants. ABC Science. 17 Dec 2009.

¹¹ NHRMC National Statement on the Ethical Conduct in Human Research 2007 (Updated 2018) E72

“Transplanting organs and tissues from animals to humans is one of the best experiments we could devise to ‘create’ new infectious agents.”¹²

The serious public biohazard of three baboons escaping from RPAH in 2020, was casually dismissed with the comical narrative that it was just two baboon “wives” accompanying the male for a vasectomy. Professor Collignon’s concerns persist.¹³ His colleagues Prof Peter Sainsbury and Prof Anne Keogh share his concerns. (personal communication)

“In most clinical trials, individual patients bear the risk of the experimental treatment, with the community benefiting from scientific knowledge gained. In Xenotransplantation this risk –benefit situation is reversed. All the benefits from xenotransplantation accrue to the individual who gets the transplantation, if it works. But most of the risk, if it occurs, goes to the community.” says Sainsbury. “So it’s a complete reversal of the normal risk-benefit analysis.”¹⁴

In the same manner donated blood is not routinely screened for COVID19, will hybrid organs be screened for unknown pathogens such as viruses and prions? There are historical precedents for medical interventions contributing to significant public health crises.

In 2016, the Journal of Infectious Diseases published “Epidemic history and iatrogenic transmission of blood-borne viruses in mid-20th century Kinshasa.” by Catherine Hogan et.al. The HIV-1 epidemic “grew more slowly before 1950, then transitioned to a much faster exponential growth sometime between 1952 and 1968.” Their findings “represent the first empirical evidence for the hypothesis that iatrogenic (Medical treatment) transmission played a role in the emergence of the HIV-1 in Kinshasa in the mid-20th Century.”¹⁵

We know that those interventions were coercive, and may have been forced on the population with the best of intentions, and yet unintended consequences can remain hidden for decades.

As Australia gears up to deal a maturing epidemic of obesity / diabetes; and a surge in cardiomyopathy following the Covid19 crisis, we may anticipate a demand for more kidneys for an aging population, and hearts for younger folk affected by an inevitable rise in autoimmune cardiomyopathy. As the NHMRC moves to expand medical procedures involving animal to human transplantation, we might all pause to consider the potential for iatrogenic harm. With 21st century technology, animal research is obsolete, misguided and has significant opportunity costs.

¹² Peter J Collignon. Controversies in Health Care. Xenotransplantation : do the risks outweigh the benefits? MJA Vol 168 18th May 1998.

¹³ Calla Wahlquist. Sydney baboon escape; the questions remain. The Guardian. 26 Feb 2020.

¹⁴ Anna Sellah see ibid see 10.

¹⁵ Catherine Hogan et.al. Epidemic history and iatrogenic transmission of blood-borne viruses in mid-20th century Kinshasa.

Our children and their grandchildren deserve due diligence with respect to protecting their genomic inheritance.

Yours sincerely,

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